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**WARNINGS**

**Fatal Infusion Reactions:** Deaths within 24 hours of RITUXAN infusion have been reported. These fatal reactions followed an infusion reaction complex which included hypoxia, pulmonary infiltrates, acute respiratory distress syndrome, myocardial infarction, ventricular fibrillation or cardiogenic shock. Approximately 80% of infusion reactions occurred in association with the first infusion. (See **WARNINGS** and **ADVERSE REACTIONS**.)

Patients who develop severe infusion reactions should have RITUXAN infusion discontinued and receive medical treatment.

**Tumor Lysis Syndrome (TLS):** Acute renal failure requiring dialysis with a fatal outcome has been reported in the setting of TLS following treatment with RITUXAN. (See **WARNINGS**.)

**Severe Mucocutaneous Reactions:** Severe mucocutaneous reactions, some with a fatal outcome, have been reported in association with RITUXAN treatment. (See **WARNINGS** and **ADVERSE REACTIONS**.)

**DESCRIPTION**



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For information on ordering Rituxan Online, please click the "online pharmacy" link on the blue horizontal navigation bar at the top of every page.

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**Written by Pharmacists**  
**Reviewed by Doctors**

**GENERIC NAME:** rituximab**BRAND NAME:** Rituxan

**DRUG CLASS AND MECHANISM:** Rituximab is an intravenous drug that is used to cell non-Hodgkin's lymphoma. It belongs to a class of drugs called monoclonal antib. Other monoclonal antibodies include trastuzumab (Herceptin) and gemtuzumab ozo (Mylotarg).

Tumor cells (like most normal cells) have receptors on their surfaces. Molecules on t of the cell can attach to these receptors. When they do, they can cause changes to c within the cells. One receptor, present in more than 90% of B-cell non-Hodgkin's lym called CD20. Molecules that attach to CD20 can affect the growth and development tumor cells and, sometimes, the production of new tumor cells. Rituximab is a man-n antibody that was developed using cloning and recombinant DNA technology from hi murine (mice or rat) genes. Rituximab is thought to attach to the CD20 receptor and tumor cells to disintegrate (lyse). In some non-Hodgkin's lymphomas, it also prevents production of more tumor cells. Rituximab was approved by the FDA in 1997.

**GENERIC AVAILABLE:** no**PRESCRIPTION:** yes

**PREPARATIONS:** Rituximab is available as a liquid in single-use vials containing 10 500mg of drug. It must be mixed with another liquid before intravenous injection. Rit free of preservatives.

**STORAGE:** Rituximab, once mixed, can be stored at 2-8°C (36-36°F) for up to 24 hc



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room temperature for up to 12 hours. The drug should be protected from sunlight.

**PRESCRIBED FOR:** Rituximab is used to treat non-Hodgkin's B-cell lymphomas that have CD20 receptors on their surface. It is used when the lymphomas recur following other therapy or are unresponsive to other types of therapy.

**DOSING:** Rituximab usually is administered once weekly for four weeks at a dose of 375 mg per meter-squared.

**DRUG INTERACTIONS:** There have been no studies of drug interactions with rituximab.

**PREGNANCY:** There are not enough studies to draw conclusions about the safety of rituximab in pregnant women. Contraceptive methods are recommended if rituximab is used in childbearing age and for up to 12 months after stopping therapy.

**NURSING MOTHERS:** Nursing mothers should avoid rituximab therapy and not breastfeed until rituximab is no longer present in the blood. Since rituximab is an antibody that can be secreted into breast milk and absorbed by the infant, it has the potential for harming infants.

**SIDE EFFECTS:** The most common side effect of rituximab is a constellation of symptoms (fever, rigors and chills) that occur during administration of the first dose of drug. More than 80% of patients experience these side effects, and it is severe in 4-7 out of every 10 patients. The side effects appear only 40% of the time with the second dose of drug; they decrease even less frequently with the last two doses. Other common side effects of rituximab are nausea, hives, fatigue, headache, itching, difficulty breathing due to bronchospasm, a sensation of swelling of the tongue or throat, runny nose, vomiting, decreased blood pressure, flushing, and pain at the site of the tumor.

After rituximab is administered, large numbers of tumor cells are immediately destroyed and eliminated from the body. In 4-5 out of every 10,000 patients the products from tumor cells cannot be eliminated quickly enough and a syndrome called tumor lysis syndrome occurs. This is characterized by a rapid decline in kidney function and a sudden accumulation of uric acid. This decrease in minerals such as potassium, calcium and phosphate to dangerous levels. Tumor lysis syndrome occurs when the size of the tumor or the number of tumor cells circulating in the blood is large, usually within 12-24 hours after the first dose of rituximab.

Irregular heart rhythms and infection are two other rarely-occurring side effects that can be severe. The irregular heart rhythm usually begins soon after the administration of the drug, while infection may develop from 30 days to 11 months after the end of therapy.

Severe decreases in red or white blood cells and platelets may occur rarely with rituximab therapy.

Rituximab therapy is not recommended if an allergy to mice or rats exists.

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## DRUGS & SUPPLEMENTS

# Rituximab (Systemic)

Drug Information provided by: Micromedex

### ARTICLE SECTIONS

- US Brand Names
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### US Brand Names

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- Rituxan

### Description

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Rituximab (ri-TUX-i-mab) is a monoclonal antibody. It is used to treat a type of cancer called non-Hodgkin's lymphoma. It can be used alone or with other cancer medicines or chemotherapy.

Rituximab is to be administered only by or under the immediate supervision of your doctor. It is available in the following dosage form:

#### Parenteral

- Injection (U.S.)

### Before Using This Medicine

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In deciding to use a medicine, the risks of taking the medicine must be weighed against the good it will do. This is a decision you and your doctor will make. For rituximab, the following should be considered:

#### Allergies

Tell your doctor if you have ever had any unusual reaction to rituximab or to mouse proteins.

#### Pregnancy

Studies on effects in pregnancy have not been done in either humans or animals. However, rituximab is related to immunoglobulin, which affects the baby's ability to fight infection and which does cross the placenta. Women who are able to bear children should use some kind of birth control during treatment with rituximab and for up to 12 months after treatment has ended. Before receiving this medicine, make sure your doctor knows if you are pregnant or if you may become pregnant.

Tell your doctor right away if you think you have become pregnant while receiving rituximab.

#### Breast-feeding

It is not known whether rituximab passes into the breast milk. However, because of the possibility of serious effects, breast-feeding is not

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recommended while you are receiving this medicine and for a while after you stop receiving it. Discuss with your doctor the proper time to begin breast-feeding after treatment with rituximab.

### Children

Studies on this medicine have been done only in adult patients, and there is no specific information comparing use of rituximab in children with use in other age groups.

### Older adults

This medicine has been tested and has not been shown to cause different side effects or problems in older people than it does in younger adults.

### Other medicines

Although certain medicines should not be used together at all, in other cases two different medicines may be used together even if an interaction might occur. In these cases, your doctor may want to change the dose, or other precautions may be necessary. When you are taking rituximab it is especially important that your doctor and pharmacist know if you are taking any of the following:

- Cisplatin (e.g., Platinol)—This medicine should not be used at the same time as rituximab because it could cause serious kidney problems

### Other medical problems

The presence of other medical problems may affect the use of rituximab. Make sure you tell your doctor if you have any other medical problems, especially:

- Heart problems (e.g., angina, arrhythmias) or
- Lung problems—Your doctor will want to check you periodically for heart and lung problems, especially if you have had serious problems in the past.
- Hepatitis B virus—Rituximab can cause the hepatitis B virus to worsen resulting in serious liver problems.
- High number of cancerous cells in your body or
- Kidney problems—You may be at higher risk for very serious unwanted effects.
- Sensitivity or a previous severe allergic reaction to rituximab or to mouse proteins—Your doctor should not administer rituximab if you have experienced a previous allergic reaction.

## Proper Use of This Medicine

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### Dosing

The dose of rituximab will be different for different patients. The dose that is used may depend on a number of things, including your weight. Rituximab is usually given by a doctor or nurse in the hospital or an outpatient clinic. If you have any questions about the proper dose of rituximab, ask your doctor.

## Side Effects of This Medicine

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Along with its needed effects, a medicine may cause some unwanted effects. Although not all of these side effects may occur, if they do occur they may need medical attention.

Check with your doctor as soon as possible if any of the following side effects occur:

### More common



Black, tarry stools; bleeding gums; bloating or swelling of face, arms, hands, lower legs or feet; blood in urine or stools; blurred vision; cough or hoarseness; dizziness; dry mouth; fatigue; feeling of swelling of tongue or throat; fever and chills; flushed, dry skin; flushing of face; fruit-like breath odor; headache; increased hunger; increased thirst; increased urination; itching; lower back or side pain; nausea; nervousness; pain or tenderness around eyes and cheekbones; painful or difficult urination; pale skin; pinpoint red spots on skin; pounding in the ears; rapid weight gain; runny nose; shortness of breath; skin rash; slow or fast heartbeat; sore throat; sores, ulcers or white spots in mouth or on lips; stuffy or runny nose; sweating; swollen glands; tightness of chest; tingling of hands or feet; troubled breathing; troubled breathing with exertion; unexplained weight gain; unusual bleeding or bruising; unusual tiredness or weakness; unusual weight gain or loss; vomiting; wheezing.

#### **Less common**

Blistering, peeling, loosening of the skin; blisters in the mouth; blisters on the trunk, scalp or other areas; burning, crawling, itching, numbness, prickling, "pins and needles", or tingling feeling; burning, tingling, numbness or pain in the hands, arms, feet, or legs; confusion; decreased frequency and amount of urination; diarrhea; difficulty in moving; discouragement; feeling sad or empty; increased thirst; irregular heartbeat; irritability; joint or muscle pain; loss of appetite; loss of interest or pleasure; muscle pain or stiffness; muscle cramps; nervousness; numbness or tingling in hands, feet, or lips; pain at place of injection; pain, swelling, or redness in joints; red, itchy lining of eye; red skin lesions, often with a purple center; stabbing pain; trouble concentrating; trouble sleeping; swelling of face or fingers; swelling of feet or lower legs; weight gain.

#### **Rare**

Chest pain.

#### **Incidence not known**

Abdominal or stomach cramps or pain; blindness; blue-yellow color blindness; blurred vision or other change in vision; burning or stinging of skin; decreased vision; dry cough; eye pain, tearing; inflammation of joints; nosebleed; pain in many joints; painful cold sores or blisters on lips, nose, eyes, or genitals; redness of eye; redness, soreness or itching of skin; sensitivity of eye to light; severe abdominal pain; severe vomiting, sometimes with blood; sores, welting, or blisters; swelling, stiffness, redness, or warmth around many joints; swollen lymph glands; vision loss; weight loss.

This medicine may also cause the following side effects that your doctor will watch for:

#### **Less common**

High blood pressure; low white blood cell count.

Other side effects may occur that usually do not need medical attention. These side effects may go away during treatment as your body adjusts to the medicine. However, check with your doctor if any of the following side effects continue or are bothersome:

#### **More common**

Back pain; fear; increased cough; joint pain; lack or loss of strength; muscle aching or cramping; night sweats; pain; pain in joints; rash; swollen joints; throat irritation.

#### **Less common**

Agitation or anxiety; change in taste; dry eyes; excessive muscle tone; feeling of constant movement of self or surroundings; feeling of weakness; general feeling of discomfort or illness; heartburn; increase in body movements; lightheadedness; muscle tension; pain at injection site; sensation of spinning; sleepiness or unusual drowsiness; swelling of



sensation of spinning, sleepiness or unusual drowsiness, swelling of stomach; trouble in sleeping.

After you stop using this medicine, it may still produce some side effects that need attention. During this period of time check with your doctor immediately if you notice any of the following:

Black, tarry stools; blood in urine or stools; painful or difficult urination; pinpoint red spots on skin; unusual bleeding or bruising; unusual tiredness or weakness.

Other side effects not listed above may also occur in some patients. If you notice any other effects, check with your doctor.

### Additional Information

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Once a medicine has been approved for marketing for a certain use, experience may show that it is also useful for other medical problems. Although these uses are not included in product labeling, rituximab is used in certain patients with the following medical conditions:

- Chronic lymphocytic leukemia (a type of cancer of the blood and lymph system)
- Waldenstrom's macroglobulinemia (a certain type of cancer of the blood)
- Immune or idiopathic thrombocytopenic purpura (ITP) (a blood disease)

Other than the above information, there is no additional information relating to proper use, precautions, or side effects for these uses.

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**ACCREDITED**



## Rituximab .com

Brand name(s) in the U.S.: Rituxan

### Product Info

#### Description

Rituximab (ri-TUX-i-mab) is a monoclonal antibody. It is used to treat a type of cancer called non-Hodgkin's lymphoma.

Rituximab is to be administered only by or under the immediate supervision of your doctor. It is available in the following dosage form:

- Parenteral*
  - Injection (U.S.)

Last Revised: 3/23/1998

Description

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## Biological therapy with monoclonal antibodies

This page tells you about treatment with monoclonal antibodies for Hodgkin's lymphoma. You can scroll down the page to read all the information here. Or use the links to go straight to sections on

- [What are monoclonal antibodies?](#)
- [Treatment with rituximab](#)
- [Other monoclonal antibodies used in NHL](#)

### What are monoclonal antibodies?

Monoclonal antibodies are a type of biological therapy. There are several different types of biological therapies, including immunotherapy. The immunotherapy used most often in lymphoma is monoclonal antibody therapy. [Monoclonal antibodies](#) (MAB's) are proteins, made in the laboratory from a single copy of a humanised antibody. MAB's are the result of many years of hard work to develop.

There are many different antibodies made by our bodies as part of the immune system's reaction to infection or damaged cells. To create a new treatment, scientists have to spend years finding an antibody that attacks the cells of one type of cancer, but does not harm normal cells. They separate out the antibody in the laboratory and then make millions of copies of it – all the same.

There are many different monoclonal antibodies being investigated for cancer treatment. Rituximab is the first one to be licensed in the UK. It is also called Mabthera or Rituxan. There are [other MAB therapies](#) being tested for NHL.

### Treatment with rituximab

Rituximab is the most common monoclonal antibody used in NHL.



- How does rituximab work?
- Who can be treated?
- Having the treatment
- Side effects

### **How does rituximab work?**

Monoclonal antibodies target one particular protein found on the surface of cells. Rituximab targets a protein called CD20. All B cells have CD20 protein on the outside of the cell. It is the B cells that are cancerous in the commonest type of low grade non Hodgkin's lymphoma. The cancerous B cells also carry the CD20 protein. The antibody sticks to all the B cells it finds. The cells of the immune system then pick out marked B cells and kill them.

B cells develop from cells in the bone marrow called stem cells. These stem cells do not have the CD20 protein. So they are not killed, and normal healthy B cells grow to replace the ones that have been killed by rituximab. Normal B cell levels in the blood are restored within a few months of having the treatment.

### **Who can be treated?**

Rituximab is licensed to treat low grade follicular NHL. This is the commonest type of low grade NHL. About 40 out of every 100 (40%) of low grade NHL's are follicular. Rituximab is used to treat low grade follicular NHL that

- Is resistant to chemotherapy
- Has relapsed at least twice after successful treatment with chemotherapy

For most people in these situations, there is no other treatment available. About half of those with follicular NHL respond to rituximab. The average time before the NHL begins to grow again is about a year. Remember this is the average – remission will be shorter in some people and longer in others. When the NHL does start to grow again you can have more rituximab treatment.

Rituximab is also used to treat people who have high grade lymphoma. In September 2003, NICE issued guidance for the treatment of large cell lymphoma, a type of high grade lymphoma. They recommend rituximab and CHOP for people with this type of lymphoma diagnosed at stage 2, 3 or 4. They don't recommend this treatment if you are not fit to have CHOP for any reason. NICE recommend that a lymphoma specialist should oversee your treatment with rituximab.



Rituximab is being tried experimentally for low grade NHL at an early stage of treatment. And other research is investigating rituximab with stem cell transplant. The rituximab gets rid of B cells that are misbehaving. The chemotherapy gets rid of the B cells that are misbehaving. It is hoped that this will reduce the risk of the cancer coming back after treatment. Our information on [what's new in NHL](#) has more about [research into rituximab for NHL](#).

### Having the treatment

You have rituximab through a drip (infusion). You will probably have to stay in overnight for your first treatment. This is because you may have a reaction to it and need some extra drugs. But after that, it is usually given in the out patients department, so you can go home after your treatment is over. You have treatment once a week for 4 weeks.

For high grade B cell lymphoma, you have rituximab with CHOP chemotherapy. You have rituximab on the first day of each cycle of CHOP, just before you have the chemotherapy.

### Side effects

All treatment has some side effects. But monoclonal antibodies do not tend to have severe side effects because they

- Are developed from proteins that occur naturally in the body
- Target cancer cells and do not attack other body cells

You are most likely to have side effects when you first have the drip. During the infusion, you may have

- Fever
- Chills and shivering (rigors)
- Feeling sick
- Itchy rash
- Headache

About half of those treated with rituximab have a reaction to it. At least one in every 20 people treated will also have

- Wheezing
- Drop in blood pressure

These side effects are most likely to come on in the first 2 hours of the first infusion. That's why you have to stay in hospital the first time you have it. The reaction can usually be prevented by having repeat



nave it. The reaction can usually be prevented by having paracetamol and an antihistamine drug before the drip starts. If you do get side effects, they can usually be controlled by slowing down the drip or stopping it for a while.

### **Other monoclonal antibodies**

Other MAB's being developed and tested for NHL include

- Ibritumomab (Zevalin)
- Tositumomab (Bexxar)
- Campath-1H
- Epratuzumab (Lymphocide)

Bexxar and Zevalin are radiolabelled monoclonal antibodies. They have a radioactive molecule attached to an anti-CD20 monoclonal antibody. The antibodies target the B cells and the radioactive molecule kills them. Because the treatment is targeted to the B cells, only a very small amount of radioactive material has to be used for each treatment. So there should be fewer side effects than with standard radiotherapy. Low blood counts seem to be the main side effect with this type of treatment. Low blood counts can cause

- Increased risk of infection
- Increased risk of bruising or abnormal bleeding
- Tiredness and shortness of breath from anaemia (shortage of red blood cells)

The blood count recovers on its own over about 2 weeks.

Zevalin is an anti-CD20 antibody connected to a molecule of radioactive yttrium (Y-90). Zevalin is now licensed for use in the UK in people with CD20 positive follicular B cell NHL who have had rituximab and it hasn't worked or their NHL has come back since their treatment. Bexxar is an anti-CD20 antibody connected to a molecule of radioactive iodine (I-131). It is being tested for use against follicular (low grade) NHL.

Epratuzumab is a monoclonal antibody that seeks out the CD22 protein. This is also found on the outside of B cells. Epratuzumab is being tested for use against follicular (low grade) NHL.

Campath-1H is a monoclonal antibody that seeks out the CD52 protein. This protein is on the outside of B and T cells. You may have this before a transplant. Or if you have a T cell lymphoma of the skin.







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## rituximab

### Trade Name(s):

Rituxan

### Type of Drug:

Rituximab is a monoclonal antibody that belongs to the general class of synthetic substances called biologic response modifiers. It is used to treat certain lymphomas that have lymphocytes with the CD20 receptor.

### How Drug Works:

A monoclonal antibody is a protein that fits like a lock and key with a protein on the cancer cell. Rituximab (antibody) attaches to the CD20 protein (antigen) on certain cancerous lymphocytes (white blood cells). Once it attaches to the cells, it brings other immune cells to help kill the cancer cells.

### How Drug Is Given:

Rituximab is given as an injection in a vein weekly for 4 weeks. The first infusion is given very slowly to see if you have a reaction. Later infusions are given a little faster if you tolerated the first one well. You will probably get other medicine to prevent a reaction if you have any trouble. The dose depends on your weight and the reason you are taking the drug. Tell your nurse if you begin to feel different at all during the treatment.

***Read the following information. If you do not understand it or if any of it causes you special concern, check with your doctor.***

### ***Before taking this drug, tell your doctor:***

- If you are trying to become pregnant, are pregnant, or breastfeeding. This drug may cause birth defects if either the male or female is taking it at the time of conception or during pregnancy. Men and women who are taking this drug need to use some kind of birth control. However, do not use oral contraceptives ("the pill") without checking with your doctor.
- If you think you may want to have children in the future. Many chemotherapy drugs can cause sterility.
- If you have any of the following medical problems: chickenpox or exposure to chickenpox, gout, heart disease, congestive heart failure, shingles, kidney stones, liver disease, or other forms of cancer.
- If you are taking any other prescription or over-the-counter drugs, including vitamins and herbals.



***Should I avoid any other medications, foods, alcohol, and/or activities?***

Your prescription and nonprescription medications may interact with other drugs, causing a harmful effect. Certain foods or alcohol can also interact with drug products. Never begin taking a new medication, prescription or nonprescription, without asking your doctor or nurse if it will interact with alcohol, foods or other medications. Some drug products can cause drowsiness and may affect activities such as driving.

**Precautions:**

While you are being treated with rituximab, and after you stop treatment, do not have any immunizations (vaccinations) without your doctor's okay. Try to avoid contact with people who have recently taken the oral polio vaccine. Check with your doctor about this.

Rituximab can often cause allergic reactions (fever and chills), especially the first treatment. Rarely, decreased blood pressure, swelling of face, and coughing can occur. Tell your nurse or doctor right away if you get a fever or chills, hives, nausea, itching, headache, shortness of breath, or swollen tongue or throat during your treatment. Your nurse will stop the infusion and evaluate you.

***Tell all the doctors, dentists, and pharmacists you visit that you are taking this drug.***

- Most of the following side effects probably will not occur.
- Your doctor or nurse will want to discuss specific care instructions with you.
- They can help you understand these side effects and help you deal with them.

**Side Effects:*****More Common Side Effects:***

- Allergic reaction with first infusion

***Less Common Side Effects:***

- Allergic reaction with second and later infusions
- Nausea
- Itching
- Hives
- Rash
- Headache
- Swelling of tongue or throat

***Rare Side Effects:***

- Tiredness (fatigue)
- Cough with shortness of breath
- Difficulty breathing
- Decreased blood pressure
- Flushing of face
- Increased heart rate



- Vomiting
- Irregular heartbeat
- Muscle aches
- Dizziness
- Decreased platelet count with increased risk of bleeding
- Decreased white blood cell count with increased risk of infection

**Side Effects/Symptoms of the Drug:**

Tell your doctor or nurse right away if you develop shortness of breath or difficulty breathing, have a fever over 100.5°F, have symptoms of infection such as coughing up sputum or burning when urinating, unusual bruising, or bleeding such as nosebleeds, bleeding of gums when you brush your teeth, or black, tarry stools.



Other side effects not listed above can also occur in some patients.

**Tell your doctor or nurse if you develop any problems.**

**FDA Approval:**

This drug is approved for cancer treatment.

**Note:** This information was adapted from the American Cancer Society's Consumers Guide to Cancer Drugs. Copyright © 2004, Jones and Bartlett Publishers. This information may not cover all possible uses, actions, precautions, side effects, or interactions, is not intended as medical advice, and should not be relied upon as a substitute for consultation with your doctor who is familiar with your medical needs. For more information, contact your American Cancer Society at 1-800-ACS-2345.

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# Rituximab

From Wikipedia, the free encyclopedia

**Rituximab**, sold under the trade names **Rituxan®** and **MabThera®**, is a monoclonal antibody used in the treatment of B cell non-Hodgkin's lymphoma and some autoimmune disorders.

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## History

Rituximab initially was approved by the FDA in 1997 for lymphoma that was refractory to other chemotherapy regimens. The original approval followed the availability of the McLaughlin *et al*<sup>[1]</sup> study data. It now is standard therapy in the initial treatment of aggressive lymphomas (e.g. diffuse large B cell lymphoma) in combination with CHOP chemotherapy.

## Mechanism

The antibody binds to the CD20 antigen found on the surface of B cells, flagging them for destruction by the body's own immune system. This eliminates B cells (including the cancerous ones) from the body, allowing a new population of healthy B cells to develop from lymphoid stem cells. The actual mechanisms for Rituximab to eliminate B cells includes the induction of ADCC, CDC, and apoptosis.

## Non-cancer use

Rituximab has been found to be effective in the treatment of immune thrombocytopenic purpura (ITP) in various trials.<sup>[2]</sup> It also seems to be effective in threatment of systemic lupus erythematosus and is being trialled in other autoimmune diseases,<sup>[3]</sup> such as rheumatoid arthritis.<sup>[4]</sup>

## References

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3. ↑ Doan T, Massarotti E. Rituximab. Drugs Today (Barc). 2005 Dec;41(12):785-97. PMID 16474854 ([http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list\\_uids=16474854](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=16474854)).
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